LEPTOSPIROSIS

The Disease as It Affects Animals

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SUMMARY

LEPTOSPIROSIS is a disease that apparently has affected animals and man since ancient times. However, the disease was first reported among cattle in the United States in 1944 and among swine in 1952. Its total economic effect is still uncertain because the exact incidence has not been determined. Effects of the disease itself vary from mild, inapparent infection to death.

In addition to cattle and swine, other animals affected may be horses, sheep, goats, dogs, and rodents.

Research on leptospirosis is aimed primarily at finding more definite means of diagnosing the disease, identifying carrier animals, and finding methods of control. The development of effective vaccines appears to give promise at this time of providing a means of control. The knowledge is not yet available to provide methods for finding and destroying all species of diseased and carrier animals that may be a continuing source of infection. The effect of treatments has not yet been fully determined. Proper herd management and sanitation are among the methods immediately available to prevent further spread of the disease.

This report deals primarily with the disease as it affects animals.

Information in this report was provided by the Animal Disease and Parasite Research Division and the Animal Disease Eradication Division, Agricultural Research Service

LEPTOSPIROSIS

Leptospirosis is a communicable disease affecting animals and man. The true economic and public health importance of the disease in this country is uncertain. However, it is becoming apparent that leptospirosis is more widespread among livestock than was previously believed, principally for two reasons: (1) More knowledge is being developed about its characteristics; and (2) as other diseases are reduced in incidence some abortions and other symptoms heretofore attributed to a disease such as brucellosis are now being traced to leptospirosis. At least, the disease is a potential threat to livestock and human health.

Leptospirosis is caused by an organism called Leptospira. About 40 species or serotypes of Leptospira have been described in various parts of the world and others may exist.

Among the animals affected are cattle, swine, horses, sheep, goats, dogs, and rodents. Perhaps a number of wild animals other than rodents may be infected with the disease or may be carriers. The disease may be transmitted from animal to man but not likely from person to person.

In many cases of infection among animals the disease causes no visible symptoms. It may cause only general unthriftiness. In more acute cases it may cause hemorrhages in various organs, abortions in pregnant cattle and swine, and nervous disorders. The liver is frequently affected and jaundice is a common symptom. When the kidneys are damaged, bloody urine is a commonly observed symptom. The disease can be fatal.

The value of currently available vaccines, cures, or treatments has not been fully determined. But proper herd management practices can reduce spread of the disease and the use of antibiotics may help to alleviate symptoms. The only means of diagnosis now available is through laboratory tests.

Research on the disease conducted by Agricultural Research Service is concentrated on Leptospira pomona, the serotype that most frequently affects cattle and swine in the United States.

DISTRIBUTION OF THE DISEASE

Leptospirosis is distributed widely throughout the world, including the United States. World reports show that the disease can reach epidemic or epizootic proportions in areas where environmental or management conditions contribute to the spread of Leptospira.

Cases of bovine leptospirosis have been encountered in every geographical region of this country, in all climatic zones, during all seasons of the year. Limited surveys have shown the disease to exist in at least

40 States among cattle and in 10 States among swine. The exact incidence of the disease is unknown.

An additional spot-check survey is being made to determine the percentage of herds in which cattle show a reaction to the agglutination test for leptospirosis. Results are expected to give a better understanding of the magnitude of the leptospiral problem in this country. Tests are being conducted by State livestock officials in 12 States and Puerto Rico in cooperation with the Animal Disease Eradication Division of ARS through the facilities of the Brucellosis Eradication Program. The plate agglutination test with L. pomona antigen is being used.

Although the tests will be made primarily on cattle in conjunction with the official brucellosis tests, facilities of the survey will be used occasionally to test other species of animals as a service to livestock owners.

The surveys have been started or will soon be started in Arizona, Colorado, Indiana, Iowa, Louisiana, Maine, Minnesota, Missouri, Montana, Nebraska, Oregon, South Carolina, and Puerto Rico.

Only about 30 human cases of leptospirosis a year are reported to the U.S. Public Health Service. However, the disease can be easily confused with such diseases as influenza, brucellosis or undulant fever, hepatitis, and meningitis. Public Health officials believe that the incidence of leptospirosis among animals influences the incidence among human beings in any given area in view of the methods of spread.

THE DISEASE ITSELF

Causative Agent

Leptospirosis is caused by a slender, spiral organism called Leptospira. The fact that it differs markedly from other agents causing infectious diseases has created some confusion concerning its exact nature, which is still in doubt. Some investigators have called the Leptospira a spirochete.

The fact that tests for leptospirosis could sometimes show a high titer and yet Leptospira could not be isolated led to an early mistaken belief that the organism might be a virus. This phenomenon is still a complicating factor in making diagnosis.

The surface of the Leptospira is bare and the ends move freely with no flagella. The organism moves spontaneously by a corkscrew motion of the ends of the one-celled organism, varying from a slow bending to a very fast rotation and forward motion. The movement of Leptospira can be seen easily through the dark field microscope.

Four serotypes of Leptospira have been identified or demonstrated as being present in the United States, and there is evidence to indicate the presence of at least four other serotypes.

The four serotypes that have been identified or demonstrated are:

1. L. pomona has been isolated from cattle, swine, and horses,

2. L. ballum has been isolated from the urine and kidneys of laboratory and house mice.

3. L. icterohaemorrhagiae has been frequently demonstrated among wild rats.

4. L. canicola has been identified in human beings, dogs, and swine; in one study, from 15 to 40 percent of the dogs tested for the presence of this serotype have reacted significantly.

The four other serotypes that are believed present, based upon collected evidence, are:

1. L. autumnalis--indicated as the cause of an outbreak of disease among soldiers at Ft. Bragg, N.C. The host has not been identified, and no further evidence of the serotype has been reported since 1944.

2. L. grippotyphosa--serological evidence reported but the serotype has not been isolated.

3. L. bataviae--serological evidence reported but the serotype has not been isolated.

4. L. sejroe--serological evidence reported but the serotype has not been isolated.

(A high titer shown by tests with antigens of specific serotypes is recognized as "serological evidence" of the presence of that serotype, even though the disease-causing agent itself is not actually isolated.)

Certain species of animals, it is believed, have a tendency to be infected with specific serotypes of Leptospira. For example, L. pomona is most frequently found to be the cause of infection in cattle; L. canicola in dogs; and rats are common carriers of L. icterohaemorrhagiae. However, sufficient exposure to any serotype may cause infection in any species. The exact relationship between specific serotypes of Leptospira and specific species of animals, either as natural or secondary carriers, is uncertain.

Man is believed to be susceptible to infection by most serotypes.

History of the Disease

Leptospirosis was first recognized as a human disease and historical reviews indicate that the infection existed in the Orient in ancient times. It spread westward into Europe by at least the eighteenth century.

It has been assumed that the acute type of jaundice that attacked Napoleon's troops during the siege of Cairo in 1800 must have been Weil's disease, caused by L. icterohaemorrhagiae. Since there is no evidence that man can contract Leptospirosis other than from direct or indirect contact with infected animals, it is further assumed that man has always contracted the disease from livestock or rodents.

Leptospira were first described in 1907 in the United States, but were mistakenly believed at that time to be the causative agent of yellow fever. It was not until 1915--in Japan and independently in Germany--that Leptospira were isolated as causative agents of Weil's disease. The following year Japanese research workers reported that the brown rat is a common carrier of L. icterohaemorrhagiae. Gradually, worldwide research has identified the other serotypes affecting the various animal species.

The first human case identified as leptospirosis in the United States was in 1922. The disease was not reported among cattle in this country until 1944 and among swine in 1952.

Methods of Spread

Leptospirosis usually attacks the kidneys and is most frequently spread from animal to animal or from animal to man through contact with infected urine or with soil, feed, water, or other materials contaminated with infected urine. Cattle have been shown to shed Leptospira in the urine for at least 3 months; dogs and swine, for much longer periods; and rodents, throughout their lifetime. Aborted fetuses and milk from acutely infected animals may be sources of infection.

Leptospira enter the body of animals and human beings through abrasions in the skin or through mucous membranes.

Epidemics of the disease among human beings have been traced to infected rats inhabiting flooded rice fields where farm workers came in contact with the Leptospira in the water. At least one outbreak among human beings in the United States was caused by swimming in water contaminated by drainage from an area where infected swine were kept.

LEPTOSPIROSIS IN CATTLE

Leptospirosis in beef and dairy cattle can vary from a mild, inapparent infection, through varying degrees of severity, to an explosive form that may terminate in death within a few days. Incubation period after artificial exposure is about 10 days.

Normally Leptospira enter the blood stream, causing fever and loss of appetite. By the end of the first week, they may pass from the blood stream and attack the kidneys; and the disease organisms then may be present in the urine for several months. The Leptospira may also attack other organs of the body, principally the liver. Jaundice is a frequent

symptom. When the organisms leave the blood stream, the temperature drops and does not usually rise again even though the Leptospira remain in the infected organs.

When it occurs, discoloration of the urine with blood may vary from a mild pink to very red or almost black. Anemia may occur as the result of loss of blood.

Milk production may be reduced or nearly stop. The milk becomes yellowish and colostrum-like and may be blood tinged. The udder may become flaccid or hardened but not inflamed. Return to normal production varies, depending in some degree upon the stage of lactation of the animal at the time the infection occurs.

Abortions may occur at any stage of pregnancy but are more usual in the last one-third. Full-term calves may be born dead or weak.

When leptospirosis becomes chronic, it may result in the stunting of young animals, reduced milk production, unthriftiness, and general debility.

Clinical symptoms of leptospirosis, when the kidneys are affected, may resemble "red water" and anaplasmosis. When the udder and milk production are affected the disease resembles mastitis; and when abortions occur it frequently resembles brucellosis. When the disease becomes chronic in a herd it may be confused with such conditions as primary malnutrition, nutritional deficiencies, parasitism, and various infectious diseases.

All symptoms are not necessarily present in a single case of leptospirosis.

LEPTOSPIROSIS IN SWINE

Leptospirosis in swine has received comparatively little attention in world research until recently, in spite of the fact that the connection of swine with the disease has long been recognized. One form of the human disease in Europe is known as "swineherd's disease."

Investigators of swine diseases in the United States during the middle 1800's reported a spirochete-like organism in their study of hog cholera, which is caused by a virus. This indicates that leptospirosis could have been present for a long time. But it was not until 1952 that the disease was first reported among swine in this country. Available information concerning its incidence today is far from complete.

Present information indicates that many leptospiral infections among swine are inapparent. But acute, explosive outbreaks of the disease and some fatal cases have been reported. The fact that bacterial and viral infections frequently occur at the same time in such outbreaks has made it difficult to be certain exactly what effects are attributable to leptospirosis alone.

Known symptoms of the disease may vary from mild jaundice and slow gains in weight to pronounced nervous and digestive disturbances. Poor appetite, fever, bloody urine, diarrhea, mild inflammation of the eyelids, and weakness of the hind legs may occur in varying degrees. When the nervous system is affected convulsive seizures have been reported.

Leptospirosis may be responsible for serious losses resulting from abortions and death of new-born pigs. In some recent investigations of abortions in sows Leptospira have been the only disease-causing organisms recovered from either the sows or aborted fetuses. This is evidence that leptospirosis is the cause of such losses.

In one outbreak of the disease in Illinois, only 85 pigs were saved from 35 sows that farrowed spring litters. Other pigs in the litters were born dead near the end of gestation period or died soon after birth. The only symptoms observed in the sows were abortion and anemia. Blood samples were positive to tests for leptospirosis.

Shoats may be unthrifty and stunted following leptospirosis. Further losses caused by the disease may occur when carcasses of hogs are condemned at the packing plant because of jaundice and anemia.

One of the most difficult problems encountered with the disease in swine is the fact that the animals shed Leptospira in the urine for long periods of time. Leptospira have been found in the urine of pigs for 6 months to 1 year after infection. Widespread inapparent infection plus the long carrier stage, therefore, can create dangerous and unsuspected reservoirs of the disease that can be spread to cattle and other animals as well as human beings. Frequently the environmental conditions and habits of swine lead to spread of the disease.

Leptospirosis in swine may resemble erysipelas, malnutrition, and various plant poisonings. When abortions occur, the disease may be confused with brucellosis.

LEPTOSPIROSIS IN OTHER ANIMALS

Sheep and Goats

Information about leptospirosis in sheep and goats in this country is exceedingly limited. In general, the symptoms resemble those of the disease in cattle.

Dogs

Canine infection is widespread in the United States. Most cases of of the disease are accompanied by at least some of the following discernible symptoms: Muscular stiffness, thirst, vomiting, dehydration, weakness, constipation or bloody diarrhea, uremic disturbances, foul breath,

jaundice, tucked-in abdomen, and arched back. Infected dogs may shed large numbers of Leptospira in the urine and are considered a frequent sources of the infection in animals and man.

Horses

The extent of infection among horses in this country is not known.

Generalized symptoms of leptospirosis may not develop in infected horses. The most usual evidence of the disease is in the eyes. The white of the eyeball and the mucous membrane lining the eyelid become red and swollen. Weakened blood vessels of the eyeball may hemorrhage and cause more permanent injury.

The condition called periodic opthalmia in horses has frequently been found in conjunction with the presence of leptospiral antibodies in the blood stream, but it has not yet been established whether the condition is due entirely to leptospirosis.

Rats and Mice

Leptospira in rats and mice, as well as in other lower animal forms, rarely cause evident disease symptoms. However, rats and mice are frequently carriers of the disease. In a survey of rats collected in about 1950 in Baltimore, 45 percent of the 1,643 rats examined were leptospiral carriers.

Large numbers of Leptospira may be concentrated in the urine of infected rats. As many as 6,000 Leptospira have been found in 1 milliliter of rat urine.

DIAGNOSIS

Clinical symptoms of leptospirosis can be observed in animals in an infected herd and may arouse suspicion of leptospirosis; but confirmed diagnosis can be made only by the isolation or demonstration of Leptospira. Practicing veterinarians can apply for diagnostic tests through the State Veterinarians in each State.

Serological tests now in use give only a presumptive rather than a definite diagnosis because the diagnostic level of titer for a positive reaction has not been unquestionably established. Indications of a positive reaction to a single test may show: (1) an infected animal, (2) one that has been infected and recovered, or (3) one that has been exposed to Leptospira and become sensitized.

When leptospirosis is suspected in a herd, serological tests are more effective in reaching a diagnosis if two or more tests are made upon samples taken 2 or 3 weeks apart to determine the trend in titer. If a significant rise in titer among a number of animals in the herd is shown by the later tests, it may be assumed that active infection is present.

A further difficulty in definite diagnosis is the fact that the disease-producing organisms frequently cannot be demonstrated in the sample material for sufficiently long periods to be isolated in the laboratory, even when the material is held under refrigeration. Therefore, it is possible to get negative cultural results for leptospirosis from an actively infected animal.

Three methods are now being used to test for leptospirosis:

(1) The agglutination-lysis test, using a live antigen, is considered the best single test for the demonstration of specific leptospiral antibodies. The principal advantage is that the serotype involved can usually be identified. The major disadvantage in the practical use of the test is that the complicated procedure is time consuming and costly. Serum from an animal is mixed with live antigen of a known leptospiral serotype. If the animal has been infected with the same serotype as that from which the antigen is prepared, the Leptospira and the leptospiral antibodies agglutinate (clump together) and then become lysed (cells destroyed). The serotype can be determined only by using a number of specific antigens because of a tendency toward cross reaction between some serotypes. (Some serotypes may show a mild reaction when placed in contact with the antigen produced by a different serotype. Determination of the Leptospira causing the infection is made on the basis of the greatest reaction to a specific antigen.)

Blood serum from animals once infected with Leptospira may react to the agglutination-lysis test for long periods after the animal has recovered from the disease. The reaction may persist for several years.

(2) The agglutination test provides a means of testing with the use of killed antigen instead of living cultures. Formalin-killed suspensions of Leptospira are most commonly used. In this test, also, the agglutination or clumping reaction determines the reading. Both agglutination plate tests and capillary tube agglutination tests are being used.

(3) The complement-fixation test can be conducted with several types of antigens, prepared in various ways. When complement is added to antigen and serum of an infected animal, the complement combines with the antigen and the leptospiral antibodies of the serum.

Reaction to the complement-fixation test usually can be demonstrated earlier in the course of the disease than the agglutination reaction but disappears much sooner. Therefore, the complement-fixation test is probably most useful in locating acute or recent infection. It is non-specific in determining the serotype of Leptospira present.

TREATMENT AND CONTROL

No completely effective methods of treatment and control have yet been developed. Clinical evidence of the disease has been reduced or eliminated following various treatments or control measures, but because leptospirosis is generally self-limiting it has been impossible to determine to what extent such treatments have contributed.

Vaccination may hold great promise as a means of controlling the disease by building up immune animal populations. Some killed vaccines have been developed but several improvements are needed before an attempt is made at general control by vaccination. Two to four weeks are required for immunity to develop following vaccination. The degree and the duration of such protection are variable. The estimated average length of immunity is about 4 months.

Antibiotics as a treatment for leptospirosis is still in the experimental stage. Some success in relieving symptoms has been reported. It is doubtful at present that the disease can be eradicated through their use, or that it is economically practical to use such treatment in controlling an infection as widespread as leptospirosis.

Herd management and sanitation offer livestock owners one of the best methods of prevention and control immediately available. General herd management affording protection against leptospirosis includes the following measures: (1) Isolate sick and aborting animals; (2) provide sanitary quarters that can be easily cleaned; (3) provide sanitary feeding and watering conditions, with special emphasis on watering tanks that prevent contamination and exposure to disease.

THE OUTLOOK

Before real progress can be made toward controlling and eradicating leptospirosis, research must provide the necessary knowledge and materials.

In addition to research programs on leptospirosis being carried out in several State agricultural experiment stations, the Animal Disease and Parasite Research Division of the Agricultural Research Service is also conducting studies at the Agricultural Research Center, Beltsville, Md.

Work at Beltsville is limited largely to L. pomona, the serotype most frequently affecting cattle and swine in the United States. Experiments are concerned with the following areas of study:

1. Growth requirements for the Leptospira in order to improve the methods of propagating the organisms for antigen and other experimental purposes. Attempts to speed the rate of growth by the addition of vitamins and other nutrients have not yet proved successful.

2. Metabolic activity of the Leptospira (the chemical and physical changes within the living cell). The more that is known about the characteristics and properties of the disease-causing agent the better the position of the research scientist to approach the problem of combating the disease.

3. Improvement of present diagnostic tests and development of new tests. The objective is to increase the accuracy and efficiency of diagnosis, including early stages of the disease, and identification of carrier animals. These will provide the means of isolating or eradicating animals capable of spreading the disease. There is a need for standardizing and improving tests to pave the way for broader testing programs.

4. Critical study of the disease as it exists naturally and under controlled conditions. Individual herd owners are permitting observations of natural outbreaks of the disease, and controlled studies are to be made at the Research Center.

There is also a need for improved vaccines that will provide an effective and more lasting immunity, as well as for more knowledge about the infecting of different species of animals with different serotypes of Leptospira.

When continuing research studies, both public and private, can solve some of these problems, an approach to successful control or eradication of leptospirosis will be possible.